REMARKS

Status of the Claims

Claims 1-7 are pending. Claim 1 is presently amended. Claims 8-9 were previously canceled.

Applicants have amended claim 1 to recite "wherein said predetermined group of pathogens comprises members of two or more genera". Support for this amendment can be found throughout the specification as filed, for example on page 10 line 20. Additional amendments to claim 1 have been made to clarify claim language. No new matter is added by these amendments.

With entry of this amendment, claims 1-7 are currently pending and under consideration.

Claim Rejections – 35 USC §103

The Examiner has rejected claims 1-5 and 7 under 35 USC 103(a) as being unpatentable over Jannes et al. in view of deSilva et al. (Action page 3). The Examiner asserts, in part, that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have extended the methods taught by Jannes to incorporate the method of determining and monitoring the temperature dependence of hybridization as taught by deSilva to arrive at the claimed invention with a reasonable expectation for success. (Action page 6)

Solely to facilitate prosecution and without acquiescence in the rejections, Applicants have amended claim 1 to recite "wherein said predetermined group of pathogens comprises members of two or more genera" (emphasis added).

However, Applicants respectfully assert that the Jannes reference is missing two elements of claim 1 as presently amended:

- "amplification and detection reaction in one reaction vessel", and
- "wherein said predetermined group of pathogens comprises members of two or more genera".

Jannes teaches methods that require multiple reaction steps and multiple reaction vessels. See Jannes Examples 1-9 which provide methods for amplification followed by a multi-step membrane-based reverse hybridization assay. In contrast, the instant invention provides methods wherein the amplification and detection of multiple genera and species take place in one reaction vessel. See page 29 in the specification as filed which provides a single 100 µl reaction mix comprising oligonucleotides

for amplification and detection of multiple genera and species. Jannes does not teach methods wherein the amplification and detection takes place in one reaction vessel.

Further, Jannes provides methods for the identification of multiple species within a single genus. See Jannes Examples 1-9 where methods for detection of species from a single genus are provided. In contrast, the instant invention provides methods for identification of a genus and species of a pathogenic organism from a predetermined group of pathogens comprising members of two or more genera. See page 30 in the specification as filed where multiple genera and species are detected. Jannes does not teach methods for identification of a pathogenic organism from a predetermined group of pathogens, wherein said predetermined group of pathogens comprises members of two or more genera.

The Examiner asserts that deSilva reference teaches an embodiment comprising step bbb, wherein deSilva provides an example of monitoring temperature dependence of hybridization. (Action page 6) Applicants respectfully submit that the deSilva reference does not correct all of the deficiencies in Jannes outlined above. deSilva teaches a method that utilizes 2 hybridization probes + a melting temperature profile for identification of a single base pair change (Factor V Leiden). deSilva does not teach the use of a plurality of hybridization reagents for the detection of multiple sequences. The present invention provides methods for identification of multiple genera and species with the use of a multiplex set of hybridization probes that detect multiple base pair changes. Claim 1 step bb) specifically requires: "a plurality of hybridization reagents, said reagents together being capable of detecting ... *all members* of said predetermined group of pathogens" (emphasis added). Further, claim 1 step b) specifically requires the "amplification and detection reaction in one reaction vessel".

Applicants assert that the teachings of deSilva cannot be applied to a plurality of hybridization reagents for the detection of two or more genera in one reaction vessel. deSilva's teachings are limited to a 2-probe system for detection of a single base pair change. It should be further noted that deSilva separately teaches detection of beta-globin sequences and Factor V Leiden sequences, however these 2 targets are amplified and detected in separate reaction vessels and there is no suggestion or motivation to analyze these sequences together in one vessel. Further, there are no teachings in deSilva directed to monitoring the temperature dependence of hybridization in a multiplex system. In contrast, the present invention provides methods for amplification and detection of all members of a predetermined group of pathogens in one reaction vessel comprising a plurality of hybridization reagents with different fluorescence properties followed by monitoring the temperature dependence of hybridization. For example, see page 16 lines 1-20, page 22 lines 29-35, and the table on page 28 in the specification as filed.

For the reasons stated above, Applicants respectfully submit that the Examiner has not established that the asserted references teach all of the claim elements.

Further, the Examiner asserts that it would have been *prima facie* obvious in view of the teachings of deSilva to "potentially ... apply the sequence specific line probes used for detection of the rRNA spacer sequences [in Jannes] to the Light Cycler format of amplification and detection". (Action page 6) As discussed above, deSilva does not provide teachings on utilizing more than 2 labeled probes in one test system. The probes as provided in Jannes were designed for use in membrane-based hybridization format, and one skilled in the art would appreciate that the probes as provided would not function in a multiplex FRET-based system.

For example, the Jannes probes were designed to be immobilized in a line-wise fashion onto a membrane strip (see Jannes Example 1). These immobilized probes do not interact with each other – they are physically separate. In contrast, probes for use in a multiplex FRET-based system would be mixed together in one reaction vessel, along with additional amplification and detection reagents; one skilled in the art would instantly appreciate that oligonucleotides together in solution could interact, forming oligo-dimers and secondary structures, etc., all of which could adversely affect the amplification and detection reactions and result in unpredictable results. Further, probes designed for FRET-based systems should have a higher melting temperature than that of the amplification primers in order to allow the probes to bind first before being displaced by the primers. Additional FRET-based probe design information can be found in the "Roche Molecular Biochemical Technical Note No. LC6/99" provided herewith on the concurrently filed Information Disclosure Statement.

The Jannes probes were designed for a different purpose which is inherently different than the function required in FRET-based system such as taught by deSilva. Neither Jannes nor deSilva provide the teachings required to achieve a multiplex FRET-based system for the identification of a pathogenic organism according to the instant invention. Applicants respectfully submit that the Examiner has not established that there would be a reasonable expectation for success in applying the probes of Jannes to the methods of deSilva, and therefore there is no motivation to extend the methods of Jannes in light of deSilva. MPEP 2143.01(v) states "if the proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion of motivation to make the proposed modification. *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (fed Cir. 1984)".

Because the Examiner has not established a *prima facie* case of obviousness, for the reasons stated above, Applicants respectfully request the reconsideration and withdrawal of the §103 rejections of claims 1-5 and 7.

The Examiner has rejected claim 6 under 35 USC 103(a) as being unpatentable over Jannes et al. in view of deSilva et al, as applied to claims 1-5 and 7 above, and further in view of Martin et al. (Action page 7). The Examiner asserts, in part, that it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have extended the teachings of Jannes and de Silva to include the additional specific types of pathogens including fungal pathogens as taught by Martin to arrive at the claimed invention with a reasonable expectation for success. (Action page 8)

As discussed above, the Examiner has not established that the Jannes and deSilva references teach all of the elements of claim 1 or its dependents, which include claim 6. The teachings of Martin do not correct these deficiencies. Thus, the Examiner has not established a *prima facie* case of obviousness based on the teachings of Jannes, deSilva and Martin.

Because the Examiner has not established a *prima facie* case of obviousness, Applicants respectfully request the reconsideration and withdrawal of the §103 rejections of claim 6.

Double Patenting

The Examiner has provisionally rejected claim 1 on the grounds of nonstatutory obviousness-type double patenting over claims 1, 2 and 6 of copending Application No. 10/534,955 in view of Jannes et al. Additionally, the Examiner has provisionally rejected claim 1 on the grounds of nonstatutory obviousness-type double patenting over claim 1 of copending Application No. 10/532,319.

If a "provisional" double patenting rejection in one application is the only rejection remaining in that application, the examiner should then withdraw the rejections and permit the application to issue as a patent. Application Nos. 10/534,955 and 10/532,319 are not currently allowed. Accordingly, Applicants submit if these provisional rejections are the only outstanding rejections, the present claims should be allowed. However, Applicants will consider filing Terminal Disclaimers when the present claims are indicated as otherwise allowable if/when Application Nos. 10/534,955 and 10/532,319 are allowed.

CONCLUSION

Applicants respectfully request entry of the present RCE and remarks. In view of the above, Applicants believe all claims now pending in this Application are in condition for allowance. If the Examiner believes that a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-730-8566.

Applicants respectfully request a 1-month extension of time to respond to the final Office Action mailed February 27, 2008. The response date was May 27, 2008; with the granting of this request, the response time is re-set to June 27, 2008.

The commissioner is hereby authorized to charge the amount of $120, the fee due under 37 CFR §1.17(a)(1) and also to charge the amount of $810, the fee pursuant to 37CFR §1.114, to Deposit Account No. 50-0812. Please grant any additional extensions of time that may be required to enter this amendment and charge any additional fees or credit any overpayments to Deposit Account No. 50-0812.

Please direct all future correspondences to: Customer No. 22829.

Respectfully submitted,

Date: 6/27/08 By: _____

Rhea C. Nersesian
Reg No. 55,488

Correspondence Address
Roche Molecular Systems, Inc.
4300 Hacienda Drive
Pleasanton, CA 94588
Tel: 925-730-8000
Fax: 925-225-1128